

# Commercialization of medical cannabis and cannabinoid-based pharmaceuticals

## Market Landscape Analysis



*Trends in legalization of medical cannabis have caused a rise in popularity of cannabinoid-based medicine. This is especially the case for the use as pain reliever. Chronic pain is one of the primary causes for missed revenue due to lost productivity (1). Popularity of cannabinoid-based pharmaceuticals is currently rising under consumers, as conventional pain relievers may deliver inadequate pain relief and adverse side-effects. This issue of Evolver market research analyzes the upcoming medical cannabis and cannabinoid pharmaceutical market.*

### **Medical Cannabis**

Several EU countries have legalized or decriminalized the medical use of cannabis to some degree (2). In 2018 several countries, including the United Kingdom, Greece, New Zealand, Germany, Canada, and several states in the U.S., legalized cannabis and the majority of Europe is expected to follow. As a result of the legalization, Europe is projected to become the largest legal cannabis market. With this increase in legalization, focus shifts towards strict control of the production of cannabis products. Creating the need for a GMP (Good Manufacturing Practice) for cannabis production. The EU-GMP standard would be good to implement globally, contributing to reduce variability in the production of medical cannabis.

There are several steps in the production process and multiple types of cannabinoids. The two most common cannabinoids are the THC (tetrahydrocannabinol) and CBD (cannabidiol), yet there are over 100 types of cannabinoids known. THC is mostly known for its recreational usage, although both THC and CBD can be used for medicinal purposes. The production of medical cannabis starts with the cultivation of the plant, followed by the harvesting, drying and curing. In the fourth step, the processing of the cannabis, the largest product variability is seen: a dried flower, an extracted oil or a future product that includes extracts, all as results of the processing (2). Therefore, the need for regulation is most needed in this phase of the production cycle.

### **Cannabinoid-based Pharmaceuticals**

Cannabinoids are the biologically active molecules responsible for the therapeutic effects observed in cannabis. It is estimated that there are over 100 different types of cannabinoids present in cannabis (3). The concentration of cannabinoid also varies between different strains of cannabis. Often, recreational strains are rich in THC or CBD, whereas specialty strains of cannabis are composed of a mix of cannabinoids. This is interesting, as Russo (2011) (4) showed that these so-called full spectrum cannabis extracts have a greater therapeutic interest than isolated or synthetic cannabinoids. This mixture of cannabinoids actually improves the treatment of chronic pain due to synergetic interactions between the different cannabis extracts (5).

Not only does cannabinoids in general, and the full spectrum cannabis extracts in particular, deliver better pain management, they are also extremely safe for consumption. This is underlined by Schaffer Library of Drug Policy (2019) (6), which states that there are no documented cannabinoid-induced fatalities: the number of overdose deaths that are attributed to conventional pain relievers, however, is steadily increasing each year (7, 8).

### *Current Chronic Pain Management*

Chronic pain is defined as pain that lasts at least three consecutive months. Chronic pain has various forms and differs significantly between individuals, with the most common pain observed in the lower-back region, or in the form of headaches and pain in extremities (9, 10). It is caused by different factors, but most commonly it is ascribed to some form of local inflammation or the presence of a neuropathic disease, e.g. multiple sclerosis (4).

A study by Breivik et al. (2006) showed that 19% of the Western population will be affected by chronic pain, whereby 21% of the research respondents were diagnosed with a depression as a result of the pain and an astonishing 61% was less able or unable to work from their homes (12). Consequently, chronic pain is one of the main causes for productivity loss and revenue loss. A recent study (13) showed that despite the availability of prescription pain medications (e.g. opioids and acetaminophen), a significant part of the patients (40%) reported an inadequate pain management. Long-term users further report experiencing several side effects, including increased pain sensitivity, withdrawal symptoms and addiction (14-19). With an estimated 130 coffins being laid to rest each day in the US alone, the conventional pain relief epidemic has become one of the leading causes of preventable deaths among 18 to 35-year-olds in Western society (20).

To overcome these side effects and improve pain management, cannabinoid pharmaceuticals are being developed. Several studies have been conducted, indicating the ability of these pharmaceuticals to relieve pain, without the side effects of the conventional pain drugs.

### The dataset

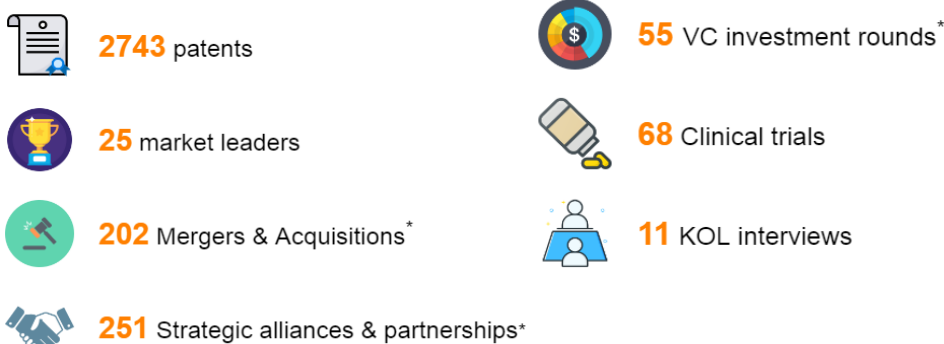


Figure 1: Dataset used for this research.

\* The chronic pain related M&A, alliance and VC deals only included a subset pertaining to cannabinoid companies, namely: 29 M&As, 87 alliances, and 8 VC investments.

### Cannabinoid Market

Pain management therapeutics is a global market with a projected compound annual growth rate of 4.0%, which is expected to increase in value from \$62 billion in 2016 to almost \$90 billion by the end of 2025 (21). Similarly, the US cannabis economy, which is currently valued at \$13 billion, is projected to increase significantly over the next 5 years, culminating in a valuation of \$24 billion in the year 2025 (22). This revenue will be generated through a combination of expenditures for medicinal marijuana, as well as recreational expenses (Figure 1). Additionally, cannabinoid pharmaceuticals could potentially increase to represent 10% of the overall specialty pharmaceutical market over the next five years, with a projected market size of at least \$20 billion (23). Moreover, the concentration of some cannabinoids, such as THC, are relatively high in comparison to other plants that are used for therapeutic purposes. The concentrations can sometimes be up to 20%, which makes the extraction of cannabinoids a more cost-effective undertaking (24) (23). Lastly, public opinion towards cannabis-derived pharmaceuticals has recently been shifting towards decriminalization and legalization in countries such as Canada and the United States, a dramatic shift compared to previous policies (25). These trends imply that cannabinoids have significant potential for successful commercialization.

### Projected growth US cannabinoid market

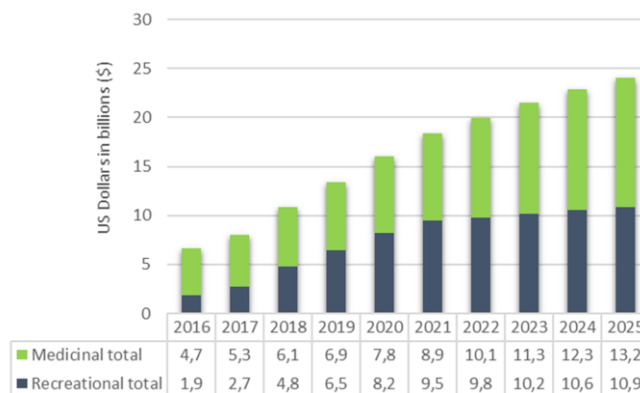


Figure 2: Growth of medicinal and recreational cannabinoid market in the US

### Cannabinoid Market Barriers

Currently, significant interest is being generated in the cannabinoid market for chronic pain relief from the bottom-up by consumers, though a lack of clinical research on the effectiveness and safety of cannabinoids has resulted in a polarized public discourse on this topic, which has created significant market barriers for their commercialization (Table 1).

To gain insights into current market trends, we have conducted interviews with several Key Opinion Leaders (KOLs). During the interviews, three market entry barriers became apparent. This includes the unfavorable legislation surrounding cannabinoids, a lack of financial incentives for pharmaceutical companies to perform clinical studies into cannabinoids and the unwillingness of healthcare providers to prescribe cannabinoids or to

reimburse their costs. KOLs overwhelmingly indicated that there is “insufficient, good quality clinical research” and that the research into cannabinoids is “completely in its infancy”.

Table 1: Market barriers for cannabinoid pharmaceuticals

Market Barriers		
Unfavorable legislation	Lack of financial incentives	Unwillingness of healthcare providers
Hard to perform clinical research, when cannabis is illegal and only non-meaningful quantities can be used for research.	Studies are costly, and because cannabis is illegal in many countries, it is hard to earn an adequate ROI. It is also hard to claim IP rights on cannabinoids.	Healthcare providers are unwilling to prescribe cannabinoids as pain relievers. Healthcare providers prefer Evidence Based Medicine (26), yet this is hard due to insufficient clinical research.

**Cannabinoid Market: The numbers**

*Cannabinoid Clinical Trials*

There are 68 clinical trials on cannabinoids as pain relieving agents that are either completed or currently running. Majority of the trials are either completed in 2019 (n = 10) or are completed in the next three years (n = 15). The number of trials is significantly less than the 3,395 clinical trials that were performed for opioids or the 988 studies that were performed for acetaminophen (Figure 3).

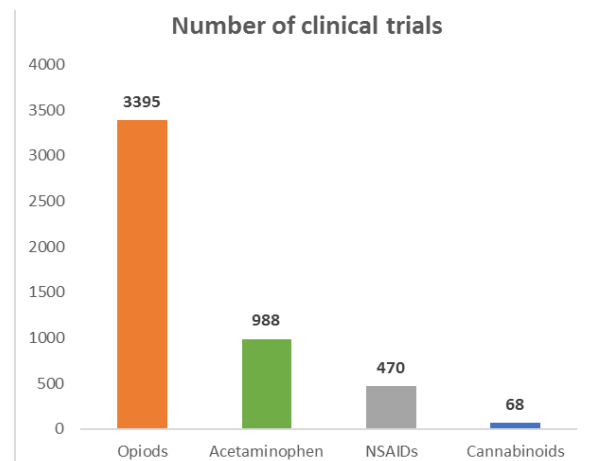


Figure 3: Cannabinoid clinical trials

The clinical trials that were conducted, were localized in four distinct regions: Canada, Europe, the Middle East and the United States (Figure 4). Interestingly, when zooming in on the specific regions, it is apparent that the number of clinical trials for cannabinoids is the highest in countries which have adopted favorable legislation for cannabinoids, legalizing their medicinal use and in some cases their recreational use, countries such as: Canada, Germany, Israel, Italy, the Netherlands, Poland, the United Kingdom and several American states including: Arizona, California and New York. This further indicates the importance of legislation for the successful commercialization of cannabinoids.

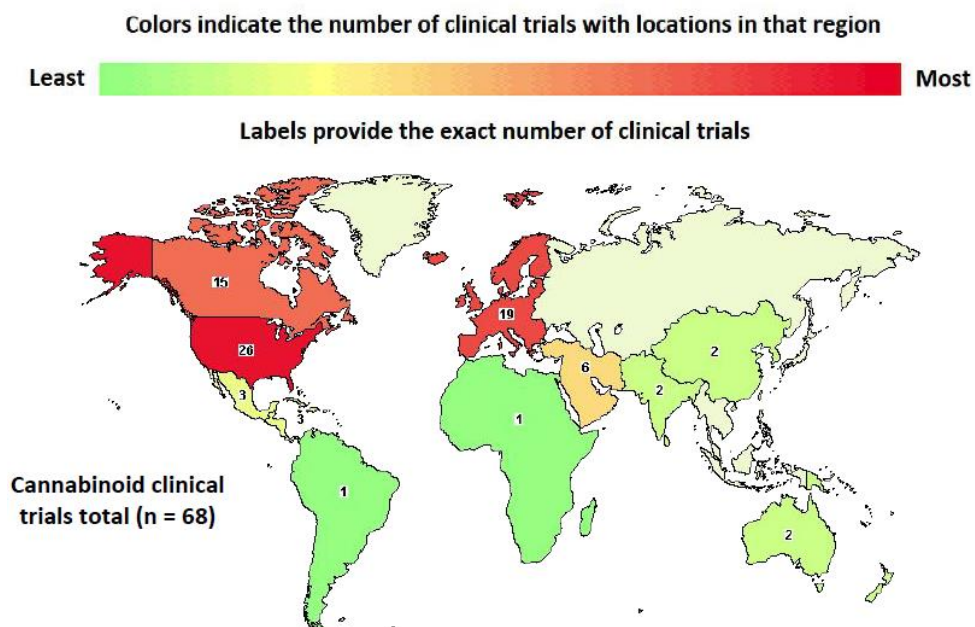


Figure 4: Location of clinical trials

**Cannabinoid Market Leaders**

The market leaders are determined based on the number of patents they own. This includes all cannabinoid patents, also the ones that are for other indications than chronic pain. The top 25 patent holders in this market are presented in Figure 5. Figure 6 shows a more detailed overview of the current patents in the field of chronic pain relief.

Additionally, when looking at the number of strategic alliances per year (Figure 7) and the major players in this area, other important players are identified, most notably Tetra Tio-Pharma Inc. with participation in 12 strategic alliances. The increase in the number of strategic alliances in the recent years between enterprises in the cannabinoid industry indicates that the industry is still in its infancy. This is further underlined by the fact that there is little Venture Capital (VC) and Merger & Acquisition (M&A) activity.

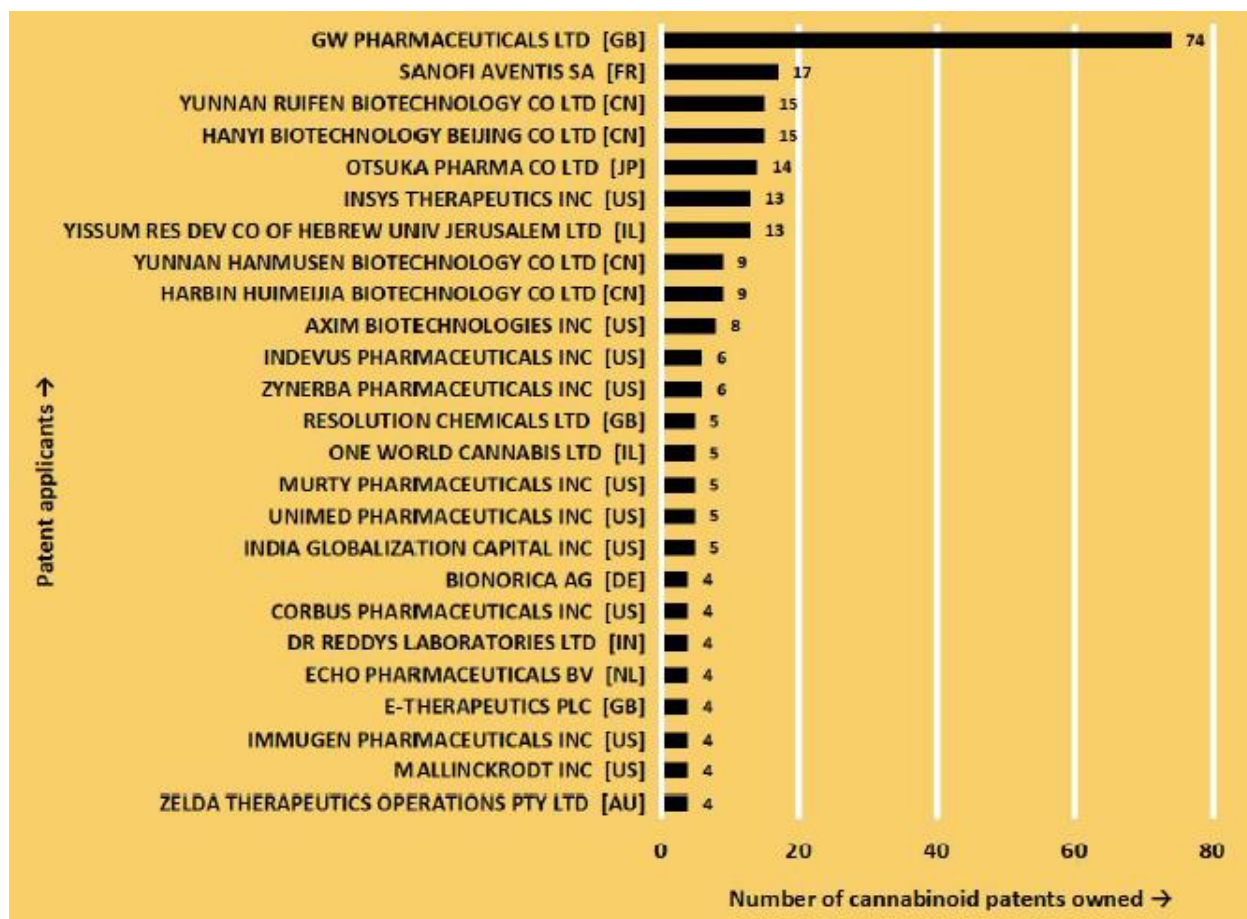


Figure 5: The top 25 patent holders in the cannabinoid field. the number of strategic alliances in this field in the last 10 years.

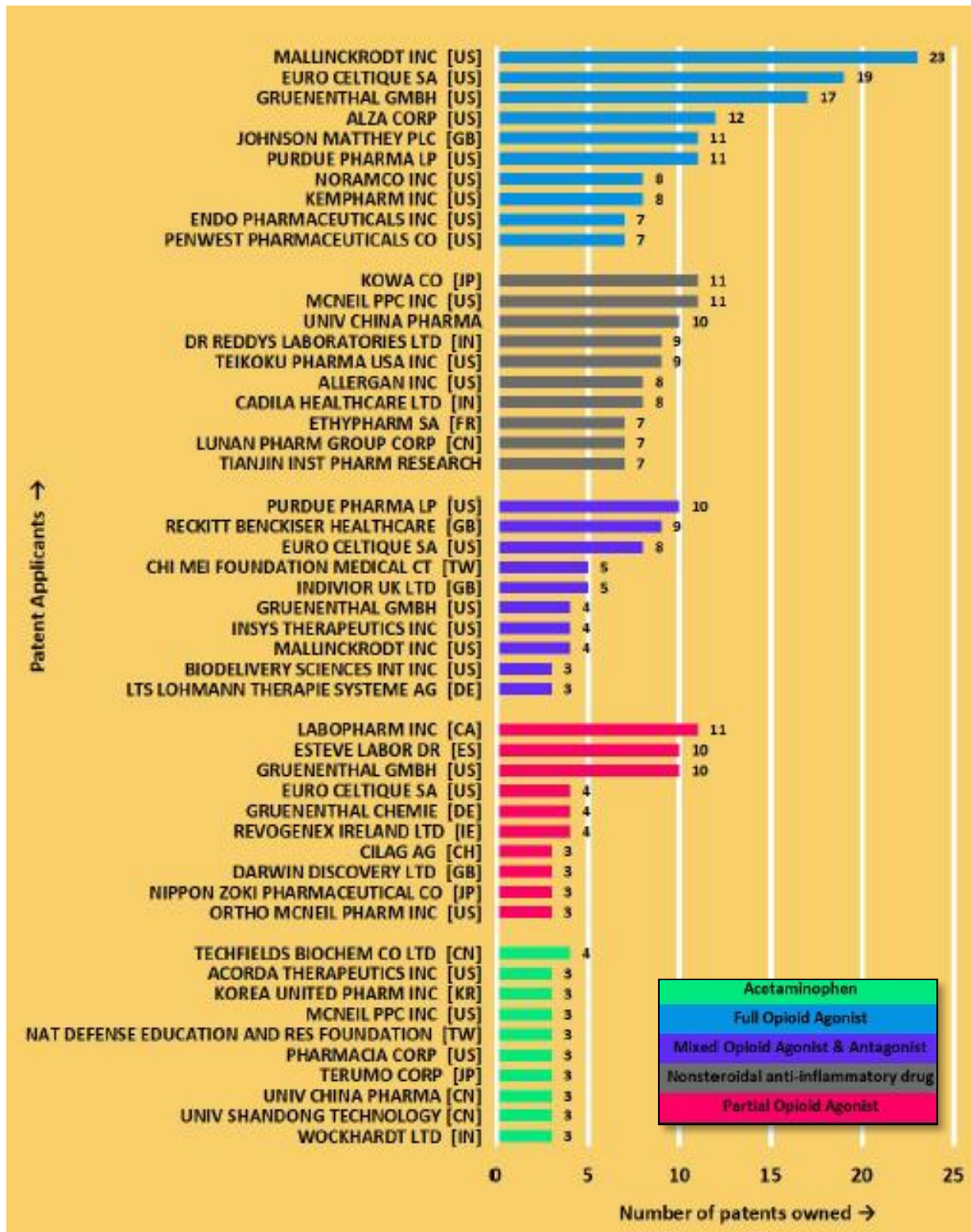


Figure 6: Patent application per area of chronic pain relief market.

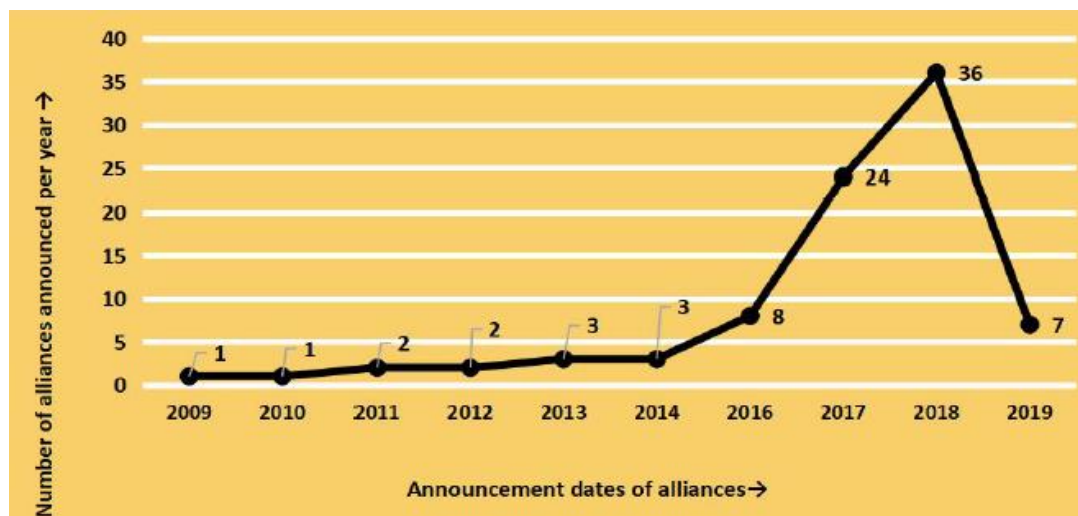


Figure 7: Number of strategic alliances over the past 10 years

### Gaps for Innovation

THC and CBD are the two cannabinoids which were found to have the highest number of patent applications, which is presumably caused by their availability in the recreational market. Therefore, specialty strains of cannabis with different compositions of cannabinoids present an interesting opportunity for innovation.

Yet, specialty cannabis strains are difficult to obtain because they must be collected from geographically isolated areas, in order to ensure that their genome has not been manipulated by humans through selective cultivation (29). Because of the difficulties to obtain and to cultivate these specialty strains, companies should encounter less barriers to claim intellectual propriety on the compositions of these strains, presenting an interesting opportunity for innovation in this market.

Enterprises can also innovate the ways how the cannabinoids are currently administered. The cannabinoids are now commonly administered through oral administration or through vaporization, even though transdermal patches would be more effective in the context of chronic pain. The common methods are not precise enough for patients to administer consistent doses of cannabinoids and some patients may be unable to use vaporizers due to a pulmonary disorders such as asthma or COPD. Interestingly, companies in the cannabinoid market are primarily focused on patenting other methods of administrations such as pharmaceuticals, edibles, and ointments.

### Final Remarks

We have looked at the medical cannabis market and in particular mapped the cannabinoid market for chronic pain relief. This industry is still in its infancy, allowing for lots of progress to be made. The unique properties of cannabinoids could allow researchers and companies to reconsider the way that clinical research is performed, which will provide additional evidence on their effectiveness and safety. Thereafter, a nuanced public discourse on this topic could be facilitated, which in turn will decrease the market barriers for the commercialization of cannabinoids for chronic pain relief. Lastly, the industry should focus on the establishment of definitive and practical strategies such that companies could pursue the commercialization of cannabinoid pharmaceuticals.

**Research accountability**

This research focussed on analysing the influence of Critical Success Factors of commercialization of cannabinoids. Trends in the last 20 years in the cannabinoid pharmaceutical markets were studied by a thorough database analysis in the form of desk research. This research consisted of a Patent, Market Leader, Merger & Acquisition, Strategic Alliances & Partnerships, Venture Capital and Clinical Trial Analysis. The databases used for this analysis included the Thomson Reuters Security Data Company (SDC) Platinum database, Espacenet and clinical trial database<sup>1</sup>. This quantitative analysis was accompanied by qualitative data by interviewing several Key Opinion Leaders in the cannabinoid pharmaceutical market.

Although our analysis aimed to be thorough, systematic and bias-free, we can in no form ensure that the data was 100% complete.

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<sup>1</sup> <https://clinicaltrials.gov/>



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